

U.S.S.N. 09/820,531

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AMENDMENT AND RESPONSE TO OFFICE ACTION**In the Claims**

21. (amended) A An improved method of detecting changes in the expression of genes associated with a particular state, disease or disorder in a microarray, wherein the genes comprise a sequence or regulatory sequence, or encode proteins or cofactors that bind to the regulatory sequence, the improvement comprising

a) providing an array of genes comprising a regulatory sequence in its promoter or interacting with a gene binding to the regulatory sequence a set of primers for reacting with a nucleic acid sequence in the genes in the microarray, with the sequence having a length of between 480 and 700 base pairs and a melting point of between 75 and 85°C; and comprising a non-consensus sequence so that there is no detectable hybridization with homologous sequences;

b) providing a reacting the set of primers for use in detecting changes in expression of genes comprising a regulatory sequence in its promoter or interacting with a gene binding to the regulatory sequence, having a length between 480 and 700 base pairs length and a melting point between 75 and 85°C, wherein the primers include non-consensus sequence with protein coding sequence so that there is no detectable hybridization between homologous genes comprising a label with the genes to amplify the nucleic acid sequence to form amplicons;

c) providing the array of genes comprising a regulatory sequence in its promoter or interacting with a gene binding to the regulatory sequence and sequences encoding proteins associated with a particular state, disease or disorder further comprising housekeeping genes

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~~whose expression does not change significantly as the state, disease or disorder changes arraying the amplicons produced from the reaction in step (b) onto a solid support; and~~

- d) reacting the primers amplicons with the genes a labeled probe comprising all or a portion of the non-consensus sequence; and
- e) detecting levels of hybridization between the amplicons and the labeled probe, thereby detecting levels of gene expression.

22. (amended) A The method of claim 21 for screening for differential expression of one or more regulatory genes or genes interacting with genes binding to the regulatory sequence, comprising:

- a) providing a first library of genes associated with a particular disease, disorder or state,
- b) providing a second library of DNA genes obtained from cells having a different state or exposed to a compound to be tested,
- c) detecting or measuring expression of selected genes in the first and second library using the method of claim 21,
- d) comparing the expression of the selected genes in the first and second libraries, and
- e) detecting which genes have altered expression in the second DNA library.

23. The method of claim 22 wherein the state is selected from the group consisting of age, cancer and diseases or disorders of the cardiovascular, neurological, musculoskeletal, systems.

24. The method of claim 22 wherein the compound is a drug or toxin.

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25. (amended) The method of claim 22 further comprising normalizing results of expression by comparison with levels of expression of housekeeping genes.
26. (amended) A The method of claim 21 for determining the effect of a compound, disease or state of an individual comprising:
 - a) providing a DNA library including one or more regulatory genes or genes interacting with genes binding to the regulatory sequence, wherein the genes are obtained from the individual after treatment of the individual, or cells or tissues derived therefrom with the compound or a particular dosage regime of the compound,
 - b) screening the library for changes in levels of expression of the selected genes using the method of claim 21, and
 - c) correlating the changes in expression with the state, disease or disorder prior to treatment.
27. The method of claim 26 wherein the cells or tissues are treated with one or more compounds *in vitro* prior to making the DNA library.
28. The method of claim 26 wherein the compound is selected from the group consisting of proteins or peptides, sugars or polysaccharides, nucleic acid molecules, and synthetic molecules.
29. The method of claim 26 wherein the library is derived from cells obtained from an individual of a particular age, having a particular disease or disorder, or derived from the neurological system, the cardiovascular system, the musculoskeletal system, or cancerous tissues.

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34. (amended) A method for screening for genes whose expression is altered by disease, age, or exogenous agent comprising screening a sample microarray comprising genes from a library, cells or animal exposed to the disease, age or exogenous agent, wherein expression of all of the genes in the microarray for binding to a microarray comprising discrete samples of nucleotide molecules hybridizing to the genes of proteins whose expression is under the control of the same regulatory element.

35. The method of claim 34 wherein the microarray further comprises control genes that are not under the control of the same regulatory element.

36. The method of claim 34 wherein the regulatory element is selected from the group of regulatory elements consisting of osmotic response element, retinoic acid response element, conserved proximal sequence element, vitamin D response element, sterol response element, TNF-alpha response element, serum response element, cAMP response element, antioxidant response element, glucocorticoid modulatory element, gonadotropin-releasing hormone-response element, pheromone response element, insulin response element, interferon consensus response element, estrogen response element, hypoxia response element, E2F transcription factor, xenobiotic response element, endoplasmic reticulum stress response element, iron-response element, androgen response element, stress response element, RAS-responsive element binding protein 1, and transforming growth factor, beta-1 response element.

37. The method of claim 34 further comprising comparing the levels of expression of the genes from a library, cells or animal exposed to the disease, age or exogenous agent, with the

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levels of expression of the genes from a library, cells or animal not exposed to the disease or exogenous agent, or of a different age.

38. The method of claim 34 wherein the disease is selected from the group consisting of neurological disorders, cardiovascular disorders, bone and muscle disorders, blood or circulation related disorders, and cancer.

39. The method of claim 38 wherein the diseases are selected from the group consisting of Alzheimer's disease, Parkinson's disease, Huntington's disease, myocardial hypertrophy, atherosclerosis, myocardial infarction, osteoarthritis, osteoporosis, and autoimmune disorders.

40. The method of claim 38 wherein the cancers are selected from the group consisting of breast cancer, prostatic hypertrophy, prostatic cancer, colon cancer, chronic lymphocytic leukemia, acute lymphocytic leukemia, brain tumors, pancreatic cancer, and hepatomas.